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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,078	09/09/2003	Gopi M. Venkatesh	451194-092	1435

7590 01/26/2007

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EXAMINER	
CHONG, YONG SOO	
ART UNIT	PAPER NUMBER
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/658,078	VENKATESH ET AL.	
	Examiner	Art Unit	
	Yong S. Chong	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 13-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 13-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/15/2006 has been entered.

Claim(s) 10-12 have been cancelled. Claim(s) 15-23 have been added. Claim(s) 1-9, 13-23 are pending. Claim(s) 1, 3, 5 have been amended. Claim(s) 1-9, 13-23 are examined herein.

Applicant's amendments have rendered the 112 rejection of the last Office Action moot, therefore hereby withdrawn. Applicant's arguments have been fully considered but found not persuasive. The rejection(s) of the last Office Action are maintained for reasons of record and modified below for Applicant's convenience.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim(s) 1-6, 8-9, 13-23 are rejected under 35 U.S.C. 103(a) as being obvious over Rampal et al. (WO 03/017981).

The instant claims are directed to an extended release tablet comprised of a macrolide antibiotic, water-soluble excipients, and a binder.

Rampel et al. teach a controlled release formulation of clarithromycin and a rate controlling cellulosic ether polymer (abstract). The composition in Example 7 is comprised of clarithromycin (84.8%), hydrophilic binder and film coat (methocel - hydroxypropylmethylcellulose) (1.75%), lactose (6.36%), magnesium stearate (1.06%), talc (0.85%), and colloidal silicon dioxide (0.43%). The composition in Example 8 is comprised of clarithromycin (84.6%), hydrophilic binder and film coat (methocel - hydroxypropylmethylcellulose) (2.35%), lactose (4.2%), water-soluble excipient (polyvinylpyrrolidone) (2.1%), magnesium stearate (1.1%), talc (0.85%), and colloidal silicon dioxide (0.40%). Other drugs such as erythromycin and its derivatives may also be used (claim 5). The tablet may be optionally film coated (claim 17), where the total weight is preferably not more than 1500 mg (claim 18). The filler can be present from 5 to 15% w/w (claim 12).

Rampel et al. disclose that cellulosic ether polymers result in extended release formulations, which release the drug over an extended period of time (pg. 2, paragraph 4). The use of the claimed amounts of rate controlling polymers not only ensures a more economical formulation compared to one made using larger amounts of polymers, it also ensures better patient compliance as patients have to take only one tablet instead of two tablets together (pg. 3, paragraph 2). Moreover, Rampel et al. disclose that cellulosic ether polymers, such as hydroxypropyl methylcellulose and hydroxypropyl cellulose, are both commercially available in a wide variety of viscosity grades and are effective in the present invention (pg. 4, paragraph 3). One particular hydroxypropyl cellulose polymer is commercially available in a wide range of viscosity grades under the trade name of Klucel® from Nippon Soda, Japan (pg. 5, second paragraph). Examiner notes that the hydroxypropyl cellulose by the trade name Klucel® is also disclosed in Applicant's disclosure as a known binder with an average viscosity of 3 to 15 cps.

Rampel et al. also teach a method of preparation in Example 7. Clarithromycin was blended with the two polymers and lactose and granulated with a solution of methocel E50 in water. The granules were dried, sized, mixed with the remaining excipients and compressed to tablets (pg. 12, lines 10-12).

However, Rampel et al. fail to specifically disclose hydroxypropylmethylcellulose or hydroxypropylcellulose having an average viscosity of 3 to 15 cps.

It would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have incorporated

hydroxypropylmethylcellulose or hydroxypropylcellulose having an average viscosity of 3 to 15 cps by the trade name, Klucel®, in the controlled release formulation disclosed by Rampel et al.

A person of ordinary skill in the art would have been motivated to incorporate hydroxypropylmethylcellulose or hydroxypropylcellulose having an average viscosity of 3 to 15 cps by the trade name, Klucel®, because: (1) Rampel et al. disclose a controlled and extended release formulation; (2) a wide variety of cellulosic ether polymers are commercially available with various viscosity grades that are known for controlled release formulation; and (3) hydroxypropylcellulose polymers under the trade name, Klucel®, has been disclosed, which possesses an average viscosity between 3 to 15 cps. Therefore, the skilled artisan would have had a reasonable expectation of success in making a controlled or extended release formulation by incorporating hydroxypropylmethylcellulose or hydroxypropylcellulose having an average viscosity of 3 to 15 cps by the trade name, Klucel®.

Generally, mere optimization of ranges will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "When the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimal or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also *In re Peterson*, 315 F. 3d at 1330, 65 USPQ 2d at 1382 "The normal desire of scientists or artisans to improve upon what is already generally known

provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." MPEP 2114.04.

Claim 7 is rejected under 35 U.S.C. 103(a) as being obvious over Rampal et al. (WO 03/017981) as applied to claims 1-6, 8-9, 13-23 in view of Vanderbist et al. (WO 02/24174 A2).

The instant claims are directed to an extended release tablet comprised of a macrolide antibiotic, water-soluble excipients, binder, and a tableting aid (microcrystalline cellulose).

Rampal et al. teach as discussed above, however fails to disclose a composition comprising microcrystalline cellulose in the amount of not more than 5% by weight.

Vanderbist et al. teach a sustained release composition containing clarithromycin (abstract) with between 5 to 50% by weight of microcrystalline cellulose (pg. 13, lines 6-8).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, for Rampal et al. to add 5% of microcrystalline cellulose to the composition as disclosed by Vanderbist et al.

A person of ordinary skill in the art would have been motivated to add microcrystalline cellulose to the composition taught by Rampel et al. because according to Vanderbist et al., excipients such as microcrystalline cellulose always guarantees the optimal dissolution of clarithromycin (pg. 7, lines 24-28).

Response to Arguments

Applicant argues that Rampel et al. does not disclose low viscosity hydroxypropyl methylcellulose polymers with an average viscosity between 3 to 15 cps. Applicant also argues that various grades have different properties and uses, therefore one of ordinary skill in the art would not interchange high with low viscosity grades for the same use.

Applicant's arguments have been fully considered but found not persuasive. Both Applicant and Rampel et al. clearly teach controlled or extended release formulations, which are controlled by the use of hydroxypropylmethylcellulose or hydroxypropylcellulose. Rampel et al. also teach that various grades of the cellulosic ether polymers are commercially available for such use. Therefore, the skilled artisan would have had a reasonable expectation of success in making a controlled or extended release formulation by incorporating hydroxypropylmethylcellulose or hydroxypropylcellulose having an average viscosity of 3 to 15 cps by the trade name, Klucel®.

It is Applicant's burden to establish unexpected results for using low viscosity cellulosic ether polymers having an average viscosity between 3 to 15 cps for use in controlled release formulations.

Regarding the establishment of unexpected results or synergism, a few notable principles are well settled. The Applicant has the initial burden to explain any proffered data and establish how any results therein should be taken to be unexpected and significant. See MPEP 716.02 (b). It is applicant's burden to present clear and convincing factual evidence of nonobviousness or unexpected results, i.e., side-by-side

comparison with the closest prior art in support of nonobviousness for the instant claimed invention over the prior art. The claims must be commensurate in the scope with any evidence of unexpected results. See MPEP 716.02 (d). With regard to synergism, a prima facie case of synergism has not been established if the data or result is not obvious. The synergism should be sufficient to overcome the obviousness, but must also be commensurate with the scope of the claims. Further, if the Applicant provides a DECLARATION UNDER 37 CFR 1.132, it must compare the claimed subject matter with the closest prior art in order to be effective to rebut a prima facie case if obviousness. See MPEP 716.02 (e).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

YSC

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER